

**FOOD AND DRUG
Research LABORATORIES, INC.**

#109

MAURICE AVENUE AT 58TH STREET, MASPETH, NEW YORK 11378



FINAL

February 26, 1973

Teratologic Evaluation of FDA 71-50

(Adipic Acid)

in

Mice, Rats, and Hamsters

Final Report-Teratologic Evaluation of FDA 71-50 (Adipic Acid) in Mice, Rats &
Hamsters
2/26/73

M I C E

Food and Drug Research Laboratories
INCORPORATED



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**F I N A L
R E P O R T**

Submitted to: DHEW/Public Health Service
Food and Drug Administration CA-272
5600 Fishers Lane-Room 5C-13
Rockville, Maryland 20852

Date February 26, 1973

Laboratory No. 1360 g
Contract No. FDA 71-260

Sample: Fine white crystalline material

Marking: FDA 71-50 (Adipic Acid)

Examination Requested: Teratologic evaluation of FDA 71-50 in mice.

Procedure: See Appendix I

Results: See Tables 1 through 4 and Appendix II

Conclusion: Subject to reexamination in the light of later findings, the following is concluded:

"The administration of up to 263 mg/kg (body weight) of the test material to pregnant mice for 10 consecutive days had no clearly discernible effect on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls."

Comment: Attention is called to the fact that this is the twenty-first of a series of reports which will be issued in accordance with the terms of the contract cited above. Eventually, a total of at least 42 compounds will have been tested in 21 pairs; each pair being run concurrently against one sham-treated control and one positive control group. Because of the inherent variability of biological data of the type dealt with here, the accumulation and pooling of sequential sets of control values will greatly enhance the statistical value of the findings and the ultimate reliability of the test results.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Kenneth Morgareidge
Kenneth Morgareidge, Ph.D.
Vice President

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FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups: 201 & 202; 207 through 210

Material: FDA 71-50

Date: January 19, 1973

Laboratory No.: 1360 g

Table 1

Fate Summary
(Mice)

Group	Material	Dose** mg/kg	Mated	Total	Surviving at Term	
					Pregnant	Total Pregnant
201	Sham	0.0	25	21	25	21
202	Aspirin*	150.0	30	21	30	21
207	FDA 71-50	2.6	25	21	25	21
208	FDA 71-50	12.0	25	23	25	23
209	FDA 71-50	56.0	25	24	25	24
210	FDA 71-50	263.0	31	20	31	20

* Positive Control : 150.0 mg/kg
 ** Administered as a water solution (10 ml per kg of body weight)

1) Includes all dams examined at term

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group : 201 & 202; 207 through 210
 Material : FDA 71-50

Date : January 19, 1973
 Laboratory No. : 1360 q

Table 2
 Reproduction Data
 (Mice)

Group :	201	202	207	208	209	210
Dose (mg/kg) :	Sham	Aspirin**	2.6	12.0	56.0	263.0
Pregnancies						
Total No.	21	21	21	23	24	20
Died or Aborted (before Day 17)	0	0	0	0	0	0
To term (on Day 17)	21	21	21	23	24	20
Corpora Lutea						
Total No.	307	331	315	293	332	364
Average/dam mated	12.3	11.4	12.6	12.7	13.3	11.7
Live Litters						
Total No.*	21	19	20	22	24	20
Implant Sites						
Total No.	242	210	250	252	289	235
Average/dam*	11.5	10.0	11.9	11.0	12.0	11.8
Resorptions						
Total No.*	9	32	27	22	12	16
Dams with 1 or more sites resorbed	8	10	11	8	10	6
Dams with all sites resorbed	--	2	1	1	--	--
Per cent partial resorptions	38.1	47.6	52.4	34.8	41.7	30.0
Per cent complete resorptions	--	9.52	4.76	4.35	--	--
Live Fetusess						
Total No.	229	178	221	229	275	214
Average/dam*	10.9	8.48	10.5	9.96	11.5	10.7
Sex ratio (M/F)	1.04	0.91	0.55	0.68	1.23	0.98
Dead Fetusess						
Total No.*	4	--	2	1	2	5
Dams with 1 or more dead	4	--	2	1	2	5
Dams with all dead	--	--	--	--	--	--
Per cent partial dead	19.1	--	9.52	4.35	8.33	25.0
Per cent all dead	--	--	--	--	--	--
Average Fetus Weight, g	0.87	0.84	0.90	0.90	0.87	0.80

* Includes only those dams examined at term.

** Positive Control : 150.0 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 201 & 202; 207 through 210Laboratory No. 1360 g

Table 3

Material FDA 71-50Date January 19, 1973Summary of Skeletal Findings*
(Mice)

<u>Findings</u>	<u>Group No.:</u>	<u>201</u>	<u>202</u>	<u>207</u>	<u>208</u>	<u>209</u>	<u>210</u>
	<u>Dose (mg/kg):</u>	<u>Sham</u>	<u>Aspirin**</u>	<u>2.6</u>	<u>12.0</u>	<u>56.0</u>	<u>263.0</u>
Live Fetuses Examined (at term)		158/21	126/19	152/20	161/22	192/24	149/20
Sternebrae							
Incomplete oss.		95/20	47/13	71/19	91/20	129/23	116/19
Scrambled							
Bipartite		3/3	3/3			5/5	5/5
Fused							
Extra					1/1		
Missing		20/7	24/9	18/9	23/9	18/8	36/10
Other							
Ribs							
Incomplete oss.							
Fused/split							
Wavy			1/1				
Less than 12							
More than 13		18/9	18/10	43/14	17/10	24/12	17/7
Other							
Vertebrae							
Incomplete oss.		8/3	16/8	3/2			
Scrambled						2/2	14/5
Fused							
Extra ctrs. oss.							
Scoliosis							
Tail defects							
Other							
Skull							
Incomplete closure		2/1					
Missing							
Craniostosis							
Other							
Extremities							
Incomplete oss.		8/3	17/8	3/3	9/5	1/1	13/5
Missing							
Extra							
Miscellaneous							
Hyoid; missing		57/16	36/14	41/15	50/14	45/16	44/14
Hyoid; reduced		23/13	18/9	21/12	35/16	41/16	31/15
Pelvic bones; incomplete					2/1		1/1

* Numerator=Number of fetuses affected; Denominator=Number of litters affected.

** Positive control: 150.0 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 201 & 202; 207 through 210Date January 19, 1973Material FDA 71-50Laboratory No. 1360 gTable 3-a
Summary of Soft Tissue Abnormalities
(Mice)

Group	Material	Dose Level mg/kg	Dam	Number of Pups	Description
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None Observed

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 201 & 202, 207 through 210Date January 19, 1973Species MiceLaboratory No. 1360 q

Table 4

Average Body Weights*

Group	Material	Dose Level	Day---				
			0	6	11	15	17**
		mg/kg	g				
201	Sham	0.0	31.2	34.2	37.7	45.2	51.6 (21)
202	Aspirin***	150.0	28.6	31.7	32.8	40.0	43.5 (21)
207	FDA 71-50	2.6	31.0	33.5	36.0	44.5	49.3 (21)
208	FDA 71-50	12.0	29.3	31.4	34.3	42.6	47.8 (23)
209	FDA 71-50	56.0	31.7	34.8	37.5	44.9	50.3 (24)
210	FDA 71-50	263.0	32.9	35.5	34.9	40.9	45.4 (20)

* Of pregnant dams

** Number of surviving dams in parentheses (c.f. Table 1)

*** Positive control: 150.0 mg/kg



Appendix I

Teratology Study in Mice

Virgin adult female albino CD-1 outbred mice were gang-housed in disposable plastic cages in temperature and humidity-controlled quarters with free access to food and fresh tap water. They were mated with young adult males, and observation of the vaginal sperm plug was considered Day 0 of gestation. Beginning on Day 6 and continuing daily through Day 15 of gestation, the females were dosed with the indicated dosages by oral intubation; the controls were sham treated.

Body weights were recorded on Days 0, 6, 11, 15, and 17 of gestation. All animals were observed daily for appearance and behavior with particular attention to food consumption and weight, in order to rule out any abnormalities which may have occurred as a result of anorexic effects in the pregnant female animal.

On Day 17 all dams were subjected to Caesarean section under surgical anesthesia, and the numbers of implantation sites, resorption sites, and live and dead fetuses were recorded. The body weights of the live pups were also recorded. The urogenital tract of each dam was examined in detail for anatomical normality.

All fetuses were examined grossly for the presence of external congenital abnormalities. One-third of the fetuses of each litter underwent detailed visceral examinations employing 10X magnification. The remaining two-thirds were cleared in potassium hydroxide (KOH), stained with alizarin red S dye and examined for skeletal defects.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 201

Material Sham

Dose 0.0 mg/kg

Date January 19, 1973

Laboratory No. 1360

Appendix II

Reproduction Data in Mice (Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Alive	Fetuses Dead	M Sex	F Sex	Resorption Sites	Average Fetus Weight (g)	Remarks
S 0601	P	16	13	12		7	5	1	0.89	----
S 0602	NP	4	0							----
S 0603	P	17	15	11	1	6	5	1	0.96	0.96
S 0604	P	14	13	11		5	8		0.75	0.92
S 0605	P	14	13	13		7	6		0.92	0.82
S 0606	P	14	13	13		3	3		0.88	0.88
S 0607	P	12	7	6	1	4	8		0.92	0.92
S 0608	P	15	12	12		3	5	1	0.94	0.94
S 0609	P	12	9	8					0.92	0.92
S 0610	NP	4	0						0.85	0.85
S 0611	P	17	13	12		8	4	1	1.00	1.00
S 0612	P	13	11	11		7	4		0.85	0.85
S 0613	P	14	12	12		7	5		0.85	0.85
S 0614	P	11	12	10	1	5	5	1	1.01	1.01
S 0615	P	15	6	6		3	3		0.77	0.77
S 0616	NP	7	0						0.79	0.79
S 0617	P	14	13	12		6	6	1	0.70	0.70
S 0618	P	13	10	10		6	4		0.86	0.86
S 0619	P	14	13	13		7	6		0.85	0.85
S 0620	P	12	11	11		8	3		0.74	0.74
S 0621	NP	0	0							----
S 0622	P	13	11	10	1	5	5		0.89	0.89
S 0623	P	15	9	9		3	6		0.89	0.89
S 0624	P	13	14	12		5	7	2	0.74	0.74
S 0625	P	14	12	11		4	7	1	0.74	0.74

* P = Pregnant; NP = Not pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 202

Material Aspirin

Dose 150.0 mg/kg

Date January 19, 1973

Laboratory No. 1360

Appendix II

Reproduction Data in Mice (Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Alive	Fetuses Dead	M Sex	N F	Resorption Sites	Average Fetus Weight (g)	Remarks
A 0601	NP	10	0							
A 0602	P	**	11	10		4	6	1	0.79	
A 0603	NP	0	0							
A 0604	NP	11	0							
A 0605	NP	15	0							
A 0606	P	10	11	10		4	6	1	1.04	
A 0607	P	15	11	11		5	6		0.82	
A 0608	P	14	11					11		
A 0609	P	12	11	11		3	8		0.70	
A 0610	P	15	13	13		6	7		0.83	
A 0611	P	9	5	3		3	0	2	1.17	
A 0612	P	13	10	10		4	6		0.85	
A 0613	P	10	9	9		5	4		0.75	
A 0614	P	14	13	13		6	7		0.87	
A 0615	P	10	9	8		4	4	1	0.62	
A 0616	P	12	11	11		7	4	1	0.78	
A 0617	P	14	7	7		6	1		1.10	
A 0618	P	13	9	9		5	4		0.90	
A 0619	NP	12	0							
A 0620	NP	9	0							
A 0621	P	14	11	10		2	8	1	0.88	
A 0622	P	12	10	9		6	3	1	0.90	
A 0623	NP	12	0							
A 0624	P	13	13	12		6	6	1	0.72	
A 0625	P	13	11	11		5	6		0.84	
A 0626	NP	11	0							
A 0627	NP	0	0							
A 0628	P	14	12					12		
A 0629	P	10	9	9		3	6		0.78	
A 0630	P	14	2	2		1	1		0.70	

* P = Pregnant; NP = Not Pregnant

** Ovary Missing

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 207

Material FDA 71-50

Dose 2.6 mg/kg

Date January 19, 1973
Laboratory No. 1360 g

Appendix II

Reproduction Data in Mice (Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex M F	Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead				
G 0001	P	13	8	8	0	0	8	1.05	
G 0002	P	14	14	14	0	6	8	0.81	
G 0003	P	16	14	12	4	8	2	0.96	
G 0004	P	13	13	4	9			1.01	
G 0005	P	12	12	3	9			0.91	
G 0006	P	12	15	12	7	5	3	0.88	
G 0007	P	15	16	15	9	6	1	0.98	
G 0008	P	13	12	11	6	5	1	0.88	
G 0009	P	12	11	10	3	7	1	0.89	
G 0010	P	10	10	10	5	5		1.12	
G 0011	P	12	5	5	2	3		1.16	
G 0012	NP	12	0					----	
G 0013	P	9	8				8		
G 0014	P	11	10	10		3	7		0.84
G 0015	NP	10	0					----	
G 0016	P	12	12	12		3	9		0.80
G 0017	P	12	11	9		1	8		0.75
G 0018	NP	9	0					----	
G 0019	P	15	12	12		3	9		0.83
G 0020	P	16	16	16		1	15		0.79
G 0021	P	15	14	12	4	8	2		0.75
G 0022	P	11	5	1		2	3		0.90
G 0023	NP	13	0					----	
G 0024	P	15	12	10	1	6	4	1	0.76
G 0025	P	13	14	13	6	7	1		0.87

* P = Pregnant; NP = Not pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 208

Material FDA 71-50

Dose 12.0 mg/kg

Date January 19, 1973

Laboratory No. 1360 g

Appendix II

Reproduction Data in Mice (Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses Alive	Fetuses Dead	Sex M	Sex F	Resorption Sites	Average Fetus Weight (g)	Remarks
G 0031	P	14	12	11		3	8	1	0.83	
G 0032	P	14	13	13		8	5		0.93	
G 0033	P	12	11	11		4	7		0.81	
G 0034	P	--**	10	10		5	5		1.02	
G 0035	P	15	11	10	1	1	9		0.69	
G 0036	P	--**	10	10		5	5		0.84	
G 0037	P	13	12	12		7	5		0.95	
G 0038	P	17	16	14		7	7	2	0.90	
G 0039	P	14	12	12		7	5		0.93	
G 0040	P	15	15	15		7	8		0.97	
G 0041	P	15	8	8		2	6		0.81	
G 0042	P	12	12	12		4	8		0.89	
G 0043	P	11	10	10		2	8		0.94	----
G 0044	NP	4	0							
G 0045	P	12	7	7		3	4		1.10	
G 0046	P	11	7	7		2	5		1.04	
G 0047	P	15	13	13		4	9		0.87	
G 0048	P	11	8	5		1	4	3	0.88	
G 0049	P	12	9	9		4	5	9	0.92	----
G 0050	P	13	9	0						
G 0051	NP	9	0							
G 0052	P	10	9	6		2	4	3	0.95	
G 0053	P	12	10	9		3	6	1	0.80	
G 0054	P	15	13	11		6	5	2	0.83	
G 0055	P	17	15	14		6	8	1	0.92	

* P = Pregnant; NP = Not Pregnant

** Ovary Missing

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 209

Material FDA 71-50

Dose 56.0 mg/kg

Date January 19, 1973

Laboratory No. 1360 g

Appendix II

Reproduction Data in Mice (Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Alive	Fetuses Dead	Sex	Resorption Sites	Average Fetus Weight (g)
G 0061	P	10	11	11		M	3	1.02
G 0062	P	14	13	13	4	F	4	0.94
G 0063	P	17	12	12	8		8	0.90
G 0064	P	16	13	13	9		9	0.75
G 0065	P	14	14	13	4		4	0.77
G 0066	P	16	15	14	6		8	0.87
G 0067	P	7	4	3	1		2	0.85
G 0068	NP	11	0					-----
G 0069	P	14	13	13	7		6	0.86
G 0070	P	18	15	15	7		8	0.91
G 0071	P	14	13	13	8		5	0.78
G 0072	P	11	9	9	5		4	0.85
G 0073	P	16	12	11	8		3	0.96
G 0074	P	13	13	12	5		7	0.80
G 0075	P	13	13	11	6		5	0.95
G 0076	P	16	17	16	10		6	0.86
G 0077	P	12	10	9	4		5	0.94
G 0078	P	16	15	14	11		3	0.86
G 0079	P	7	2	1	0		1	0.64
G 0080	P	12	12	12	9		3	0.83
G 0081	P	11	12	11	7		4	0.85
G 0082	P	12	11	11	6		5	0.80
G 0083	P	14	14	14	4		10	1.10
G 0084	P	16	15	15	9		6	0.93
G 0085	P	12	11	9	4		5	0.78

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 210Material FDA 71-50Dose 263.0 mg/kgDate January 19, 1973Laboratory No. 1360 g

Appendix II

Reproduction Data in Mice

(Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	<u>Fetuses</u>	Sex	Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive Dead	M F			
G 0091	P	16	2			1	1.04	
G 0092	P	15	16	16		10	0.84	
G 0093	P	14	6	4	2	6	0.81	
G 0094	P	14	13	12	1	2	0.77	
G 0095	P	18	15	15	4	11	0.84	
G 0096	P	13	10	10	7	3	0.88	
G 0097	NP	3	0				----	
G 0098	P	15	13	12	1	6	0.71	
G 0099	P	12	13	12	5	7	0.87	
G 0100	P	19	14	14	10	4	0.80	
G 0101	P	15	13	13	7	6	0.83	
G 0102	P	13	12	12	7	5	0.78	
G 0103	NP	13	0				----	
G 0104	NP	0	0				----	
G 0105	NP	12	0				----	
G 0106	P	11	11	10	1	6	0.68	
G 0107	P	13	14	13	5	8	0.90	
G 0108	P	12	12	12	6	6	0.89	
G 0109	P	15	12	1	1	0	0.55	
G 0110	NP	14	0				----	
G 0111	P	14	11	11			0.81	
G 0112	P	14	13	12	1	4	0.51	
G 0113	NP	0	0				----	
G 0114	NP	14	0				----	
G 0115	NP	12	0				----	
G 0116	NP	14	0				----	
G 0117	P	13	12	11			0.71	

Continued on next page.

* P = Pregnant; NP = Not Pregnant

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**F I N A L
R E P O R T**

Submitted to: DHEW/Public Health Service
Food and Drug Administration CA-272
5600 Fishers Lane-Room 5C-13
Rockville, Maryland 20852

Date February 26, 1973

Laboratory No. 1361 g
Contract No. FDA 71-260

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Marking: FDA 71-50 (Adipic Acid)

Examination Requested: Teratologic evaluation of FDA 71-50 in rats

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"The administration of up to 288 mg/kg (body weight) of the test material to pregnant rats for 10 consecutive days had no clearly discernible effect on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls."

Comment: Attention is called to the fact that this is the twenty-first of a series of reports which will be issued in accordance with the terms of the contract cited above. Eventually, a total of at least 42 compounds will have been tested in 21 pairs; each pair being run concurrently against one sham-treated control and one positive control group. Because of the inherent variability of biological data of the type dealt with here, the accumulation and pooling of sequential sets of control values will greatly enhance the statistical value of the findings and the ultimate reliability of the test results.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Kenneth Morgareidge
Kenneth Morgareidge, Ph.D.
Vice President

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FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups: 201 & 202; 207 through 210

Date: January 19, 1973

Material: FDA 71-50

Laboratory No.: 1361 g

Table 1

Fate Summary
(Rats)

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			Mated	Pregnant	Total	Pregnant
201	Sham	0.0	25	20	25	20
202	Aspirin*	250.0	28	24	27	23
207	FDA 71-50	2.9	25	23	25	23
208	FDA 71-50	13.0	25	24	25	24
209	FDA 71-50	62.0	25	22	25	22
210	FDA 71-50	288.0	24	20	24	20

* Positive Control : 250.0 mg/kg

** Administered as a water solution (See Appendix I)

1) Includes all dams examined at term

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group : 201 & 202; 207 through 210
 Material : FDA 71-50

Date : January 19, 1973

Laboratory No. : 13619

Table 2

Reproduction Data

(Rats)

Group :	201	202	207	208	209	210
Dose (mg/kg) :	Sham	Aspirin**	2.9	13.0	62.0	288.0
Pregnancies						
Total No.	20	24	23	24	22	20
Died or Aborted (before Day 20)	0	1	0	0	0	0
To term (on Day 20)	20	23	23	24	22	20
Corpora Lutea						
Total No.	292	264	314	303	279	263
Average/dam mated	11.7	10.2	12.6	12.1	11.2	11.4
Live Litters						
Total No.*	20	17	23	24	22	20
Implant Sites						
Total No.	227	238	260	254	245	230
Average/dam*	11.4	10.4	11.3	10.6	11.1	11.5
Resorptions						
Total No.*	2	81	6	3	--	7
Dams with 1 or more sites resorbed	2	12	1	2	--	3
Dams with all sites resorbed	--	4	--	--	--	--
Per cent partial resorptions	10.0	52.2	4.35	8.33	--	15.0
Per cent complete resorptions	--	17.4	--	--	--	--
Live Fetuses						
Total No.	224	150	254	248	245	223
Average/dam*	11.2	6.52	11.0	10.3	11.1	11.2
Sex ratio (M/F)	0.85	0.88	1.00	0.89	1.02	0.99
Dead Fetuses						
Total No.*	1	7	--	3	--	--
Dams with 1 or more dead	1	4	--	3	--	--
Dams with all dead	--	--	--	--	--	--
Per cent partial dead	5.00	17.4	--	12.5	--	--
Per cent all dead	--	--	--	--	--	--
Average Fetus Weight, g	3.88	2.46	3.89	3.83	4.01	3.99

* Includes only those dams examined at term.

** Positive Control : 250.0 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 201 & 202; 207 through 210 Laboratory No. 1361 g

Table 3

Material FDA 71-50 Date January 19, 1973Summary of Skeletal Findings*
(Rats)

Findings	Group No.:	201	202	207	208	209	210
	Dose (mg/kg):	Sham	Aspirin**				
Live Fetuses Examined (at term)		159/20	100/16 ^a	176/23	175/24	171/22	157/20
Sternebrae							
Incomplete oss.		66/19	80/16	46/18	60/13	61/17	44/15
Scrambled							
Bipartite		1/1	7/5	1/1	1/1	1/1	1/1
Fused			1/1				
Extra							
Missing		17/8	85/16	20/9	4/3	7/2	9/5
Other							
Ribs							
Incomplete oss.							
Fused/split			10/5				
Wavy		16/7	45/14	12/5	26/11	12/7	29/10
Less than 12							
More than 13		1/1	81/13	6/3	1/1	5/3	
Other							
Vertebrae							
Incomplete oss.		20/10	92/16	19/8	25/9	12/7	19/8
Scrambled			1/1				
Fused							
Extra ctrs. oss.							
Scoliosis			1/1				
Tail defects							
Other							
Skull							
Incomplete closure		21/11	43/15	25/12	35/10	23/11	26/11
Missing			9/3				
Craniostosis							
Other							
Extremities							
Incomplete oss.			4/3				
Missing							
Extra							
Miscellaneous							
Hyoid; missing		19/8	52/15	14/9	26/12	23/10	19/11
Hyoid; reduced		3/3	7/5	18/8	24/10	18/12	24/11

* Numerator=Number of fetuses affected; Denominator=Number of litters affected.

** Positive control: 250.0 mg/kg

a) One litter lost in processing

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 201 & 202; 207 through 210Date January 19, 1973Material FDA 71-50Laboratory No. 1361 a

Table 3-a
Summary of Soft Tissue Abnormalities
(Rats)

Group	Material	Dose Level mg/kg	Dam	Number of Pups	Description
202	Aspirin*	250.0	A 1614	4	Encephalomyelocele
				1	Encephalomyelocele; umbilical hernia
			A 1619	1	Encephalomyelocele
			A 1625	1	Meningoencephalocele
				1	Encephalomyelocele
			A 1626	1	Encephalomyelocele; umbilical hernia
				2	Meningoencephalocele
			A 1628	1	Encephalomyelocele; umbilical hernia
208	FDA 71-50	13.0	G 1032	1	Meningoencephalocele

* Positive Control: 250.0 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 201 & 202; 207 through 210Date January 19, 1973Species Rats

Table 4

Laboratory No. 1361 q

Average Body Weights*

Group	Material	Dose Level	Day---				Day---
			0	6	11	15	
		mg/kg	g				
201	Sham	0.0	215	240	253	276	344 (20)
202	Aspirin**	250.0	215	238	249	264	303 (23)
207	FDA 71-50	2.9	213	235	251	272	336 (23)
208	FDA 71-50	13.0	214	235	247	271	332 (24)
209	FDA 71-50	62.0	214	237	253	274	340 (22)
210	FDA 71-50	288.0	217	239	253	273	343 (20)

* Of pregnant dams

** Number of surviving dams in parentheses (c.f. Table 1)

*** Positive control: 250.0 mg/kg



Appendix I

Teratology Study in Rats

Virgin adult female albino rats (Wistar derived stock) were individually housed in mesh bottom cages in temperature and humidity-controlled quarters with free access to food and fresh tap water. They were mated with young adult males, and observation of the vaginal sperm plug was considered Day 0 of gestation. Beginning on Day 6 and continuing daily through Day 15 of gestation, the females were dosed with the indicated dosages by oral intubations. The controls were sham treated with the vehicle at a level equivalent to the group receiving the highest test dose. The test material was prepared and doses calculated according to the following table:

Dosage (mg/kg)	Dose (ml/kg)	Concentration (mg/ml)
≤ 250	1	≤ 250
251 - 500	2	125 - 250
501 - 750	3	133 - 250
751 - 1000	4	187 - 250
1001 - 1250	5	200 - 250
1251 - 1500	6	208 - 250
1501 - 1600	6.4	235 - 250

Body weights were recorded on Days 0, 6, 11, 15, and 20 of gestation. All animals were observed daily for appearance and behavior with particular attention to food consumption and weight, in order to rule out any abnormalities which may have occurred as a result of anorexic effects in the pregnant female animal.

On Day 20 all dams were subjected to Caesarean section under surgical anesthesia, and the numbers of implantation sites, resorption sites, and live and dead fetuses were recorded. The body weights of the live pups were also recorded. The urogenital tract of each dam



was examined in detail for anatomical normality.

All fetuses were examined grossly for the presence of external congenital abnormalities. One-third of the fetuses of each litter underwent detailed visceral examinations employing 10X magnification. The remaining two-thirds were cleared in potassium hydroxide (KOH), stained with alizarin red S dye and examined for skeletal defects.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 201Material ShamDose 0.0 mg/kgDate January 19, 1973Laboratory No. 1361

Appendix II

Reproduction Data in Rats (Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Alive	Fetuses Dead	M	Sex F	Resorption Sites	Average Fetus Weight (g)	Remarks
S 1601	P	9	8	8		3	5		4.03	
S 1602	P	16	15	15		3	12		3.74	
S 1603	NP	4	0						---	
S 1604	P	11	12	11		4	7	1	3.76	
S 1605	NP	10	0						---	
S 1606	NP	8	0						---	
S 1607	P	13	12	12		6	6		3.55	
S 1608	P	11	11	11		6	5		3.84	
S 1609	P	13	13	13		5	8		3.63	
S 1610	P	12	11	11		5	6		3.75	
S 1611	P	10	10	10		3	7		3.88	
S 1612	P	13	11	11		6	5		3.44	
S 1613	P	14	14	13	1	8	5		3.66	
S 1614	NP	8	0						---	
S 1615	P	12	12	12		7	5		3.95	
S 1616	P	16	12	12		4	8		4.28	
S 1617	NP	7	0						---	
S 1618	P	14	11	11		6	5		3.85	
S 1619	P	14	11	11		6	5		3.81	
S 1620	P	12	11	11		4	7	1	3.58	
S 1621	P	14	11	10		4	6		3.61	
S 1622	P	15	11	11		5	6		3.64	
S 1623	P	14	13	13		7	6		5.61	
S 1624	P	12	11	11		7	4		3.74	
S 1625	P	10	7	7		4	3		4.15	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 202Material AspirinDose 250.0 mg/kgDate January 19, 1973Laboratory No. 1361

Appendix II

Reproduction Data in Rats
(Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses Alive	Fetuses Dead	Sex M	Sex F	Resorption Sites	Average Fetus Weight (g)	Remarks
A 1601	P	16	16	8	8	8	8	5	3.00	
A 1602	P	12	7	2		5	3	5	----	
A 1603	P	10	8						2.11	
A 1604	NP	15	0						----	
A 1605	P	13	13	4	9				2.98	
A 1606	NP	0	0						----	
A 1607	P	4	12					12	----	
A 1608	P	8	5			3	2		2.71	
A 1609	P	12	12	5	7	5	7		2.54	
A 1610	P	7	7	2	5	2	5		2.79	
A 1611	P	11	10	4	6	4	6		1.57	
A 1612	P	10	10	4	6	4	6		2.89	
A 1613	P	9	9	3	6	3	6		2.90	
A 1614	P	12	13	5	7	1			2.05	
A 1615										Not Assigned
A 1616	P	14	13	4	9			11	3.28	
A 1617	P	----	11						----	Aborted Day 15
A 1618	NP	9	0						----	
A 1619	P	----	5	3			2		----	
A 1620	NP	4	0					10	----	
A 1621	P	8	10							2.20
A 1622	P	14	11	11		6	5			
A 1623	P	13	12	3	0	3	0	9	2.16	
A 1624	P	13	11	3	0	3	0	8	1.93	
A 1625	P	9	11	9	1	6	3	2	2.12	
A 1626	P	10	12	8	1	4	4	3	1.87	
A 1627	P	9	10					10	----	
A 1628	P	10	8	1	1	1	0	6	2.77	
A 1629	P	12	13					13	----	

* P = Pregnant; NP = Not Pregnant

** Ovary Missing

*** Not Read

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 207Material FDA 71-50Dose 2.9 mg/kgDate January 19, 1973Laboratory No. 1361g

Appendix II

Reproduction Data in Rats

(Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses Alive	Fetuses Dead	Sex M	Sex F	Resorption Sites	Average Fetus Weight (g)	Remarks
G 1001	P	11	11	11	0	6	5	5	3.77	
G 1002	P	11	11	11	0	6	5	5	4.03	
G 1003	P	14	13	13	0	5	8	5	3.76	
G 1004	P	13	12	12	0	5	7	5	3.84	
G 1005	P	11	13	7	0	6	1	6	3.48	
G 1006	P	15	15	15	0	7	8	7	3.80	
G 1007	NP	13	0	0	0	---	---	---	---	
G 1008	P	12	12	12	0	6	6	6	3.97	
G 1009	P	15	14	14	0	5	9	5	4.14	
G 1010	P	12	11	11	0	9	2	9	3.65	
G 1011	P	10	10	10	0	4	6	4	3.63	
G 1012	P	10	7	7	0	5	2	5	4.04	
G 1013	P	10	9	9	0	4	5	4	5.18	
G 1014	P	6	5	5	0	1	4	1	3.73	
G 1015	P	16	12	12	0	9	3	9	3.98	
G 1016	P	12	12	12	0	7	5	7	3.98	
G 1017	P	15	12	12	0	4	8	4	4.08	
G 1018	P	14	12	12	0	8	4	8	3.84	
G 1019	P	15	12	12	0	4	8	4	3.85	
G 1020	NP	9	0	0	0	6	4	6	3.70	
G 1021	P	13	10	10	0	5	7	5	3.91	
G 1022	P	13	12	12	0	6	5	6	3.90	
G 1023	P	14	11	11	0	4	9	4	3.73	
G 1024	P	14	13	13	0	5	6	5	3.45	
G 1025	P	16	11	11	0	---	---	---	---	

* P = Pregnant; NP = Not pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 208

Material FDA 71-50

Dose 13.0 mg/kg

Date January 19, 1973

Laboratory No. 1361 g

Appendix II

Reproduction Data in Rats (Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex M F	Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead				
G 1031	P	13	13	10	1	6	7	4.39	
G 1032	P	12	11	5	9	3	7	3.88	
G 1033	P	14	14	14	0	4	6	3.40	
G 1034	P	10	10	10	0	5	7	3.67	
G 1035	P	14	12	12	0	5	7	3.56	
G 1036	P	13	13	13	0	8	5	3.62	
G 1037	P	11	6	6	0	2	4	3.73	
G 1038	P	9	9	9	0	6	3	3.86	
G 1039	P	9	9	9	0	3	6	4.50	
G 1040	P	11	11	11	0	6	5	4.03	
G 1041	P	10	10	10	0	7	3	4.35	
F 1042	P	10	9	8	1	6	2	4.14	
G 1043	P	13	13	12	1	4	8	3.65	
G 1044	P	13	12	12	0	6	6	3.26	
G 1045	P	15	13	13	0	7	6	3.67	
G 1046	NP	10	0	0	0	2	4	4.32	
G 1047	P	17	6	6	0	5	4	3.99	
G 1048	P	12	9	1	0	3	6	3.78	
G 1049	P	13	9	9	0	5	5	3.37	
G 1050	P	13	10	10	0	5	4	3.83	
G 1051	P	11	9	9	0	3	7	3.41	
G 1052	P	11	10	10	0	5	6	4.03	
G 1053	P	13	11	11	0	4	7	3.76	
G 1054	P	13	11	11	0	7	4		
G 1055	P	13	11	11	0	7	4	3.69	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 209Material FDA 71-50Dose 62.0 mg/kgDate January 19, 1973Laboratory No. 1361 g

Appendix II

Reproduction Data in Rats
(Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex M F	Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead				
G 1061	P	12	11	11	5	5	6	4.13	
G 1062	P	8	5	5	0	2	3	4.21	
G 1063	P	11	10	10	0	4	6	3.84	
G 1064	P	14	13	13	0	6	7	3.86	
G 1065	P	12	12	12	0	4	8	4.11	
G 1066	P	7	7	7	0	1	6	3.79	
G 1067	P	16	16	16	0	6	10	3.61	
G 1068	P	12	12	12	0	6	6	3.80	
G 1069	NP	7	0	0	0	12	3	-----	
G 1070	P	15	15	15	0	5	6	3.90	
G 1071	P	12	11	11	0	5	6	4.02	
G 1072	P	14	12	12	0	5	7	3.65	
G 1073	P	14	14	14	0	8	6	4.04	
G 1074	P	13	13	13	0	10	3	4.10	
G 1075	P	14	12	12	0	5	7	3.77	
G 1076	NP	0	0	0	0	6	7	-----	
G 1077	P	14	13	13	0	3	5	3.83	
G 1078	P	8	8	8	0	0	1	4.14	
G 1079	P	9	1	1	0	0	0	5.25	
G 1080	NP	4	0	0	0	8	6	4.03	
G 1081	P	14	14	14	0	7	6	4.28	
G 1082	P	14	13	13	0	10	3	4.04	
G 1083	P	14	13	13	0	6	6	3.95	
G 1084	P	12	12	12	0	5	3	3.77	
G 1085	P	9	8	8	0	8	8	-----	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 210

Material FDA 71-50

Dose 288.0 mg/kgDate January 19, 1973
Laboratory No. 1361 g

Appendix II

Reproduction Data in Rats

(Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses	Alive	Dead	Sex M F	Resorption Sites	Average Fetus Weight (g)	Remarks
G 1091	P	8	8	8	0	0	3 5	3	3.85	Not Assigned
G 1092	P	16	15	15	0	0	8 7	8	3.90	
G 1093	P	12	11	11	0	0	6 5	6	3.95	
G 1094	P	11	11	11	0	0	6 5	6	3.94	
G 1095	P	14	14	14	0	0	6 8	6	4.02	
G 1096	P	10	7	7	0	0	4 3	4	4.05	
G 1097	P	7	7	7	0	0	4 3	4	4.05	
G 1098	NP	0	0	0	0	0	----	----	----	
G 1099	P	15	15	15	0	0	4 11	4	3.82	
G 1100	P	13	13	13	0	0	8 5	8	3.88	
G 1101	P	11	11	11	0	0	3 8	3	3.70	
G 1102	P	17	15	15	0	0	8 7	8	4.28	
G 1103	P	10	10	10	0	0	5 5	5	4.29	
G 1104	P	13	12	12	0	0	8 4	8	3.92	
G 1105	P	10	10	10	0	0	4 6	4	5.60	
G 1106	NP	6	0	0	0	0	----	----	----	
G 1107	P	16	14	14	0	0	9 5	9	3.78	
G 1108	NP	12	0	0	0	0	----	----	----	
G 1109	P	----**	11	11	0	0	6 5	6	3.76	
G 1110	P	15	9	9	0	0	4 5	4	4.09	
G 1111	P	12	11	11	0	0	4 7	4	3.94	
G 1112	P	12	12	12	0	0	7 4	7	3.67	
G 1113	NP	5	0	0	0	0	----	----	----	
G 1114	P	11	11	11	0	0	6 4	6	4.04	
G 1115	P	7	10	5	5	5	2 3	2	3.23	

* P = Pregnant; NP = Not Pregnant

** Ovary Missing

HAMSTERS

Food and Drug Research Laboratories
INCORPORATED



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**FINAL
REPORT**

Submitted to: DHEW/Public Health Service
Food and Drug Administration CA-272
5600 Fishers Lane-Room 5C-13
Rockville, Maryland 20852

Date February 26, 1973

Laboratory No. 1362 g
Contract No. FDA 71-260

Sample: Fine white crystalline material

Marking: FDA 71-50 (Adipic Acid)

Examination Requested: Teratologic evaluation of FDA 71-50 in hamsters

Procedure: See Appendix I

Results: See Tables 1 through 4 and Appendix II

Conclusion: Subject to reexamination in the light of later findings, the following is concluded:

"The administration of up to 205 mg/kg (body weight) of the test material to pregnant hamsters for 5 consecutive days had no clearly discernible effect on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls."

Comment: Attention is called to the fact that this is the twenty-first of a series of reports which will be issued in accordance with the terms of the contract cited above. Eventually, a total of at least 42 compounds will have been tested in 21 pairs; each pair being run concurrently against one sham-treated control and one positive control group. Because of the inherent variability of biological data of the type dealt with here, the accumulation and pooling of sequential sets of control values will greatly enhance the statistical value of the findings and the ultimate reliability of the test results.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Kenneth Morgareide
Kenneth Morgareide, Ph.D.
Vice President

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FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups: 201 & 202; 207 through 210

Date: January 19, 1973

Material: FDA 71-50

Laboratory No.: 1362 q

Table 1

Fate Summary
(Hamsters)

Group	Material	Dose ** mg/kg	Total		Surviving at Term Pregnant	
			Mated	Pregnant	Total	Pregnant
201	Sham	0.0	25	24	25	24
202	Aspirin*	250.0	25	24	25	24
207	FDA 71-50	2.0	25	21	23	19
208	FDA 71-50	9.5	27	22	26	21
209	FDA 71-50	44.0	25	23	25	23
210	FDA 71-50	205.0	26	22	26	22

* Positive Control : 250.0 mg/kg

** Administered as a water solution (See Appendix I)

1) Includes all dams examined at term

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group : 201 & 202; 207 through 210
 Material : FDA 71-50

Date : January 19, 1973
 Laboratory No. : 1362 q

Table 2
 Reproduction Data
 (Hamsters)

Group :	201	202	207	208	209	210
Dose (mg/kg) :	Sham	Aspirin**	2.0	9.5	44.0	205.0
Pregnancies						
Total No.	24	24	21	22	23	22
Died or Aborted (before Day 14)	0	0	2	1	0	0
To term (on Day 14)	24	24	19	21	23	22
Corpora Lutea						
Total No.	329	291	292	312	309	286
Average/dam mated	13.2	12.1	12.2	11.6	12.4	11.4
Live Litters						
Total No.*	24	24	19	21	23	21
Implant Sites						
Total No.	314	290	246	267	298	271
Average/dam*	13.1	12.1	13.0	12.7	13.0	12.3
Resorptions						
Total No.*	11	17	5	4	6	21
Dams with 1 or more sites resorbed	5	9	4	3	5	7
Dams with all sites resorbed	--	--	--	--	--	1
Per cent partial resorptions	20.8	37.5	21.1	14.3	21.7	31.8
Per cent complete resorptions	--	--	--	--	--	4.55
Live Fetus es						
Total No.	303	273	240	262	291	250
Average/dam*	12.6	11.4	12.6	12.5	12.7	11.4
Sex ratio (M/F)	0.64	0.63	0.78	0.85	0.72	0.84
Dead Fetus es						
Total No.*	--	--	1	1	1	--
Dams with 1 or more dead	--	--	1	1	1	--
Dams with all dead	--	--	--	--	--	--
Per cent partial dead	--	--	5.26	4.76	4.35	--
Per cent all dead	--	--	--	--	--	--
Average Fetus Weight, g	1.70	1.75	1.75	1.73	1.70	1.75

* Includes only those dams examined at term.

** Positive Control : 250.0 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 201 & 202; 207 through 210 Laboratory No. 1362 g

Table 3

Material FDA 71-50

Date January 19, 1973Summary of Skeletal Findings*
(Hamsters)

Findings	Group No.:	201	202	207	208	209	210
	Dose (mg/kg):	Sham	Aspirin**				
Live Fetuses Examined (at term)		211/24	188/24	166/19	183/21	199/23	173/21
Sternebrae							
Incomplete oss.		76/21	77/22	53/18	62/21	108/23	49/16
Scrambled							
Bipartite		39/14	33/18	22/13	30/16	13/11	25/16
Fused							
Extra						1/1	
Missing		44/16	31/12	25/12	29/13	38/14	23/10
Other							
Ribs							
Incomplete oss.							
Fused/split			1/1				1/1
Wavy							
Less than 12		1/1					
More than 13		43/17	36/13	32/13	32/15	32/15	48/18
Other							
Vertebrae							
Incomplete oss.		11/8	6/5	2/2	3/3	4/3	9/5
Scrambled							
Fused							
Extra ctrs. oss.					1/1		
Scoliosis					1/1		1/1
Tail defects							
Other							
Skull							
Incomplete closure		1/1					1/1
Missing					1/1		
Craniostosis							
Other							
Extremities							
Incomplete oss.		62/20	44/15	20/10	13/7	44/16	30/9
Missing							
Extra							
Miscellaneous							
Hyoid; missing		4/4	1/1	1/1		7/4	3/3
Hyoid; reduced		5/4	6/4	5/4	2/2	9/6	5/2
Pelvic bones; missing							2/2

* Numerator=Number of fetuses affected; Denominator=Number of litters affected.

** Positive control: 250.0 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 201 & 202; 207 through 210Date January 19, 1973Material FDA 71-50Laboratory No. 1362 gTable 3-a
Summary of Soft Tissue Abnormalities
(Hamsters)

Group	Material	Dose Level mg/kg	Dam	Number of Pups	Description
201	Sham	0.0	S 2618	9	Meningoencephalocele
208	FDA 71-50	9.5	G 2033	1	Meningoencephalocele

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 201 & 202; 207 through 210

Date January 19, 1973

Table 4

Species Hamsters

Laboratory No. 1362 g

Average Body Weights*

Group	Material	Dose Level	0	6	8	10	14**
		mg/kg	g				
201	Sham	0.0	109.2	114.1	118.8	130.2	153.1 (24)
202	Aspirin***	250.0	104.5	110.1	117.6	124.9	145.2 (24)
207	FDA 71-50	2.0	102.2	108.8	112.7	123.9	148.1 (19)
208	FDA 71-50	9.5	109.9	114.6	118.2	128.5	151.0 (21)
209	FDA 71-50	44.0	104.0	108.9	112.4	122.0	142.7 (23)
210	FDA 71-50	205.0	102.8	107.1	111.0	121.0	140.8 (22)

* Of pregnant dams

** Number of surviving dams in parentheses (c.f. Table 1)

*** Positive control: 250.0 mg/kg



Appendix I

Teratology Study in Hamsters

Virgin adult female golden hamsters from an outbred strain were individually housed in mesh bottom cages in temperature and humidity controlled quarters with free access to food and fresh tap water at all times. They were mated (1 to 1) with mature males and the appearance of motile sperm in the vaginal smear was considered as Day 0 of gestation. Beginning on Day 6 and continuing daily through Day 10 of gestation, the indicated dose levels of the test material were administered by oral intubation. The controls were sham treated with the vehicle at a level equivalent to the group receiving the highest test dose. The test material was prepared and doses calculated according to the following table:

Dosage (mg/kg)	Dose (ml/kg)	Concentration (mg/ml)
≤ 250	1	≤ 250
251 - 500	2	125 - 250
501 - 750	3	133 - 250
751 - 1000	4	187 - 250
1001 - 1250	5	200 - 250
1251 - 1500	6	208 - 250
1501 - 1600	6.4	235 - 250

Body weights were recorded on Days 0, 8, 10, and 14 of the gestation period. All animals were observed daily for appearance and behavior with particular attention to food consumption in order to better recognize any abnormalities resulting from anorexic effects in the pregnant animal.

On Day 14, all animals were subjected to Caesarian section under deep anesthesia and the numbers of implantation sites, resorption



sites, live and dead fetuses were recorded. All live pups were weighed and the genital tract of each dam was examined for any anatomical abnormalities.

All fetuses were examined grossly for the presence of external congenital defects and one-third of each litter underwent detailed visceral examination under 10X magnification. The remaining two-thirds of the pups were cleared in potassium hydroxide, stained with alizarin red dye, and examined for the presence of skeletal abnormalities.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 201

Material Sham

Dose 0.0 mg/kg

Date January 19, 1973

Laboratory No. 1362

Appendix II

Reproduction Data in Hamsters (Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses Alive	Fetuses Dead	Sex M	Sex F	Resorption Sites	Average Fetus Weight (g)	Remarks
S 2601	P	14	13	13		6	7		1.84	
S 2602	NP	9	0							
S 2603	P	14	13	13		7	6		1.69	
S 2604	P	10	10	10		8	2		1.75	
S 2605	P	15	16	16		8	8		1.51	
S 2606	P	11	11	11		3	8		1.39	
S 2607	P	12	13	9		2	7	4	1.79	
S 2608	P	14	13	13		3	10		1.88	
S 2609	P	15	15	15		7	8		1.85	
S 2610	P	14	13	13		6	7		1.59	
S 2611	P	16	15	15		3	12	1	1.56	
S 2612	P	12	12	11		2	9	2	1.89	
S 2613	P	10	11	9		1	8	2	1.56	
S 2614	P	15	14	14		8	6		1.61	
S 2615	P	13	12	12		7	5		1.72	
S 2616	P	11	11	11		3	8		1.76	
S 2617	P	13	13	13		5	8		1.68	
S 2618	P	12	13	10		4	6	3	1.56	
S 2619	P	13	13	13		4	9		1.76	
S 2620	P	15	15	15		4	11		1.68	
S 2621	P	16	15	14		6	8	1	1.78	
S 2622	P	14	14	14		1	13		1.67	
S 2623	P	14	13	13		9	4		1.78	
S 2624	P	13	13	13		5	8		1.73	
S 2625	P	14	13	13		6	7		1.77	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 202Material AspirinDose 250.0 mg/kgDate January 19, 1973

Appendix II

Reproduction Data in Hamsters (Individual)

Laboratory No. 1362

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses Alive	Fetuses Dead	Sex M/F	Resorption Sites	Average Fetus Weight (g)	Remarks
A 2601	P	12	12	12		6/6	6	1.76	
A 2602	P	11	11	11		4/7	4	1.46	
A 2603	P	11	10	10		4/6	4	1.76	
A 2604	P	11	12	10		7/3	2	1.70	
A 2605	P	14	15	13		5/8	2	1.87	
A 2606	P	10	10	9		3/6	1	1.86	
A 2607	P	11	12	10		4/6	2	1.86	
A 2608	P	10	11	9		1/8	2	1.53	
A 2609	P	16	15	15		6/9	6	1.82	
A 2610	P	16	16	16		4/12	2	1.75	
A 2611	P	14	16	14		3/11	2	1.96	
A 2612	P	5	3	3		0/3	0	1.78	
A 2613	P	15	14	14		3/11	3	1.86	
A 2614	P	14	15	13		6/7	2	1.79	
A 2615	P	13	14	11		6/5	3	1.76	
A 2616	P	12	12	12		6/6	6	1.57	
A 2617	P	14	13	13		9/4	4	1.74	
A 2618	P	12	12	12		4/8	8	1.86	
A 2619	P	13	12	12		5/7	7	1.69	
A 2620	P	12	11	11		1/10	1	1.68	
A 2621	NP	11	0						---
A 2622	P	--**	10	9		4/5	1	1.79	
A 2623	P	11	11	11		4/4	7	1.90	
A 2624	P	10	10	10		4/4	6	1.78	
A 2625	P	13	13	13		6/6	7	1.54	

* P = Pregnant; NP = Not Pregnant

** Not Read

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 207

Material FDA 71-50

Dose 2.0 mg/kg

Date January 19, 1973
 Reproduction Data in Hamsters (Individual) Laboratory No. 1362 g

Appendix II

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses Alive	Fetuses Dead	Sex M	Sex F	Resorption Sites	Average Fetus Weight (g)	Remarks
Reproduction Data in Hamsters (Individual)										
G 2001	P	9	9			4	5			
G 2002	P	13	13	1.3		6	7			1.77
G 2003	NP	6	0							----
G 2004	P	11	10	10		5	5			1.70
G 2005	P	10	9	8	1	2	6			1.55
G 2006	P	14	14	14		4	10			1.77
G 2007	P	14	15	13		2	11	2		1.44
G 2008	P	10	10	9		3	6	1		1.74
G 2009	NP	0	0							----
G 2010	P	15	13	1.3		8	5			1.86
G 2011	P	14	14	14		5	9			1.92
G 2012	P	15	15	15		4	11			1.94
G 2013	P	14	14	14		8	6			----
G 2014	P	13	13	13		8	5			1.90
G 2015	P	13	12	12		5	7			1.73
G 2016	NP	---	0							----
G 2017	P	12	12	12		8	4			1.97
G 2018	P	16	16	16		7	9			1.51
G 2019	P	15	14	13		3	10	1		1.79
G 2020	P	13	13	13		9	4			1.83
G 2021	NP	11	0							----
G 2022	P	13	13	13		3	10			1.73
G 2023	P	12	12	12		8	4			1.60
G 2024	P	15	15	14		7	7	1		1.65
G 2025	P	14	13	13		8	5			1.76

* P = Pregnant; NP = Not Pregnant

** Not Readable

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 208

Material FDA 71-50

Dose 9.5 mg/kg

Date January 19, 1973
Laboratory No. 1362 g

Appendix II

Reproduction Data in Hamsters (Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses Alive	Fetuses Dead	Sex M	Sex F	Resorption Sites	Average Fetus Weight (g)	Remarks
G 2031	P	12	11	11		7	4		1.62	
G 2032	P	10	10	10		4	6		1.74	
G 2033	P	10	9	9		3	6		1.61	
G 2034	P	11	11	11		7	4		1.74	
G 2035	P	14	14	14		4	10		1.73	
G 2036	P	11	11	11		4	7		1.52	
G 2037	NP	4	0						----	
G 2038	P	18	18	18		11	7		1.81	
G 2039	P	11	11	11		7	4		1.70	
G 2040	NP	2	0						----	
G 2041	P	11	12	11	1	2	9		1.56	
G 2042	P	15	14	14		8	6		1.78	
G 2043	P	12	12	12		7	5		1.81	
G 2044	P	10	10	10		3	7		1.83	
G 2045	NP	8	0						----	
G 2046	NP	4	0						----	
G 2047	P	15	16	15		6	9	1	1.67	
G 2048	P	13	13	13		6	7		1.75	
G 2049	NP	5	0						----	
G 2050	P	13	13	13		7	4	2	1.73	
G 2051	P	12	12	12		7	5		1.77	
G 2052	P	9	--	--		--	--		----	
G 2053	P	15	14	14		6	8		1.77	
G 2054	P	11	11	11		5	6		1.79	
G 2055	P	24	20	19		6	13	1	1.87	
G 2056	P	14	11	11		6	5		1.69	
G 2057	P	18	14	14		4	10		1.79	
G 2058	P									Not Assigned

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 209Material FDA 71-50Dose 44.0 mg/kgDate January 19, 1973
Laboratory No. 1362 g

Appendix II

Reproduction Data in Hamsters (Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses Alive	Fetuses Dead	Sex M	Sex F	Resorption Sites	Average Fetus Weight (g)	Remarks
G 2061	P	12	13	11		6	5	2	1.85	
G 2062	P	14	14	14		9	5		1.59	
G 2063	P	10	11	10	1	2	8		1.62	
G 2064	P	14	14	14		5	9		1.46	
G 2065	NP	0	0						----	
G 2066	P	11	11	11		3	8		1.74	
G 2067	P	13	12	12		3	9		1.76	
G 2068	P	12	12	12		6	6		1.65	
G 2069	P	13	12	12		3	9		1.63	
G 2070	P	17	15	15		9	6		1.60	
G 2071	NP	7	0						----	
G 2072	P	12	12	11		3	8	1	1.68	
G 2073	P	17	17	17		9	8		1.61	
G 2074	P	12	12	12		8	4		1.90	
G 2075	P	13	12	12		5	7		1.67	
G 2076	P	14	14	14		5	9		1.58	
G 2077	P	15	15	15		5	10		1.55	
G 2078	P	13	14	13		2	11	1	1.69	
G 2079	P	12	11	10		5	5	1	1.68	
G 2080	P	15	15	15		9	6		1.90	
G 2081	P	12	11	10		4	6		1.66	
G 2082	P	12	12	12		4	8		1.85	
G 2083	P	13	13	13		5	7		1.68	
G 2084	P	13	13	13		7	6		1.76	
G 2085	P	13	13	13		4	9		1.90	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 210

Material FDA 71-50

Dose 205.0 mg/kg

Date January 19, 1973

Laboratory No. 1362 g

Appendix II

Reproduction Data in Hamsters (Individual)

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses Alive	Fetuses Dead	Sex M	Sex F	Resorption Sites	Average Fetus Weight (g)	Remarks
G 2091	P	11	11			6	5		1.88	----
G 2092	NP	0	0							----
G 2093	NP	0	0							----
G 2094	P	13	12					3	9	1.65
G 2095	P	14	14					6	7	1.57
G 2096	P	10	10					5	5	1.86
G 2097	P	12	12					6	6	1.86
G 2098	P	11	11					5	6	1.85
G 2099	P	11	11					4	7	1.99
G 2100	P	14	13					5	8	1.70
G 2101	P	12	12					3	9	1.80
G 2102	P	14	14					5	9	1.82
G 2103	P	10	12					6	4	1.80
G 2104	P	12	12					5	6	1.58
G 2105	P	10	9					6	3	1.91
G 2106	P	14	12					6	5	1.66
G 2107	P	12	14					1	14	----
G 2108										Not Assigned
G 2109	NP	8	0							----
G 2110	P	13	13					6	6	1.64
G 2111	P	14	14					7	6	1.66
G 2112	P	12	12					6	6	1.89
G 2113	NP	---	0							----
G 2114	P	12	12					12	12	1.63
G 2115	P	12	12					12	5	1.83
G 2116	P	19	15					15	7	1.43
G 2117	P	16	14					14	6	1.65

* P = Pregnant; NP = Not Pregnant